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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BLANCHARD, DAVID J	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,207	KANDIMALLA ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-54* is/are pending in the application.

4a) Of the above claim(s) *27,30-33,36-38,41-46 and 50-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,28,29,34,35,39,40 and 47-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 October 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendments filed 27 October 2003, 7 April 2004, 22 July 2004 and 6 September 2005 have been entered in full.

2. Claims 26-54 are pending.

Election/Restrictions

3. Applicant's election of the invention of Group IV, claims 34-35 and 47-49 in the reply filed on 17 May 2007 is acknowledged. It is noted that the restriction requirement mailed 7/12/2007 identifies that claims 26-29 and 39-41 as linking claims, however, claims 27 and 41 are not linking claims because they recite specific embodiments unique to the linked inventions and as such are not generic to each of the linked groups of inventions, i.e., groups I-IV. The linking claims, i.e., claims 26, 28-29 and 39-40, will be examined with the elected invention of Group IV. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 27, 30-33, 36-38, 41-46 and 50-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

5. Claims 26, 28-29, 34-35, 39-40 and 47-49 are under consideration.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 09 February 2004 has been fully considered by the examiner. A signed and initialed copy of the IDS is included with the instant Office Action.

Specification

7. The cross reference to related applications at pg. 1 of the specification needs to be updated to indicate that the present application is a divisional of USSN 09/965,116,

filed 9/26/2001. Applicant is advised that USSN 09/965,116 is allowed, but not yet issue and should be updated with the corresponding US Patent No. when available during the pendency of the present application. Applicant is reminded that priority application USSN 09/965,116 cannot be incorporated by reference after the original filing of the instant application. See United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003) "Benefit of Prior-Filed Application" (see Part VII). Additionally, the status of USSN 09/712,898 needs to be updated as "now abandoned".

8. The examiner acknowledges applicants amendment to the description of the figures filed 10/25/2006, however, the amendment is objected to because the parts of Figures 1-26 (i.e., parts A, B, C) are not described in the Brief description of the Figures. "For example, if the drawings show Figures 1A, 1B, and 1C and the brief description of the drawings refers only to Figure 1, this is an error in the specification which must be corrected, rather than an application filed without all figures of drawings." See MPEP 601.01(g).

9. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 26, 28-29, 34-35, 39-40 and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied

through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2163).

In the instant case, the claims are directed to generating an immune response or treating cancer in a patient comprising administering an immunostimulatory oligonucleotide compound comprising an immunostimulatory dinucleotide of formula 5'-pyrimidine-purine-3', wherein the pyrimidine is a non-natural pyrimidine nucleoside and the purine is a natural or non-natural purine nucleoside and wherein the immunostimulatory dinucleotide is conjugated to an antigen or vaccine wherein conjugation is to the 3'-end of the oligonucleotide compound and wherein the immunostimulatory oligonucleotide is administered with a chemotherapeutic agent.

The specification teaches (pg. 11) that the term "immunostimulatory oligonucleotide compound" means a compound comprising an immunostimulatory dinucleotide, without which the compound would not have an immunostimulatory effect. The specification discloses that CpG is one such immunostimulatory dinucleotide and sets forth CpG immunostimulatory dinucleotide analogs comprising a cytosine analog or a guanosine analog (pg. 12). Further, the specification discloses that cytosine has two hydrogen bond acceptor groups at positions 2 (keto-oxygen) and 3(nitrogen), and a hydrogen bond donor group at the 4-position (amino group), wherein these groups serve as potential recognizing and interacting groups with receptors that are responsible for immune stimulation and sets forth specific cytosine analogs (e.g., see Fig. 28 and Table 2). In contrast to the written description set forth in the present application, the structure of the immunostimulatory oligonucleotides comprising an immunostimulatory dinucleotide of the formula 5'-pyrimidine-purine-3', wherein the pyrimidine is a non-natural pyrimidine nucleoside and the purine is a natural or non-natural purine nucleoside is vast in view of the numerous non-natural pyrimidine nucleosides and

natural or non-natural purine nucleosides and in view of the open claim language of "comprising" which indicates that there are other structural components to the claimed immunostimulatory oligonucleotides. See MPEP 2111.03. The structures of the immunostimulatory oligonucleotides comprising the immunostimulatory dinucleotide 5'-pyrimidine-purine-3' wherein the pyrimidine is a non-natural pyrimidine nucleoside and purine is a natural or non-natural purine nucleoside are not known and is inclusive to a variety of subgenera that differ structurally and functionally. For example, the written description of the present application does not describe a representative number of species of immunostimulatory oligonucleotides comprising the immunostimulatory dinucleotide CpA, TpA, TpG, wherein the pyrimidine is a non-natural pyrimidine and the purine is a natural or non-natural purine. The claims do not set forth the specific structure of the immunostimulatory oligonucleotides and immunostimulatory dinucleotide generically having the formula 5'-pyrimidine-purine-3' wherein the pyrimidine is a non-natural pyrimidine nucleoside and the purine is a natural or non-natural purine nucleoside such that one skilled in the art would recognize that the applicants' invented the claimed subject matter.

A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]. " See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the

one disclosed." For example, the specification discloses that a hydrophobic substitution at the 5-position of cytosine completely suppresses immunostimulatory activity of a CpG-oligo (see pg. 29). The written description does not set forth a representative number of species of immunostimulatory oligonucleotides comprising an immunostimulatory dinucleotide having the formula 5'-pyrimidine-purine-3' wherein the pyrimidine is a non-natural pyrimidine nucleoside and the purine is a natural or non-natural purine nucleoside, particularly immunostimulatory dinucleotides CpA, TpA, TpG as embraced by the generic formula 5'-pyrimidine-purine-3', and wherein the immunostimulatory oligonucleotides generate an immune response or treat cancer in patient. Verthelyi et al (The Journal of Immunology, 168:1659-1663, 2002) states that "[D]ue to evolutionary divergence in CpG recognition between species, ODN that are highly active in rodents are poorly immunostimulatory in primates, and vice versa" (e.g., pg. 1659, left col.) and "CpG ODN that activate human immune cells in vitro are only weakly immunostimulatory in mice" (e.g., pg. 1662, Discussion, first par.). Dittmer et al (Current Opinion in Microbiology, 6:472-477, 2003) reports that "[U]nfortunately, CpG-ODN that optimally stimulate mouse cells were only weakly effective in human cells, thus they could not be used for the treatment of humans" (e.g., pg. 472, right col., bottom par.). Thus, one of skill in the art could not predict the operability of any other species of immunostimulatory oligonucleotides comprising an immunostimulatory dinucleotide having the formula 5'-pyrimidine-purine-3' wherein the pyrimidine is a non-natural pyrimidine nucleoside and purine is a natural or non-natural purine nucleoside other than those disclosed.

Further, it is not sufficient to define a substance solely by its principal biological property, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Per the *Enzo* court's example, (*Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (CA FC 2002) at 1616) of a description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) couched "in terms of its function of lessening inflammation of tissues" which, the court stated, "fails to distinguish any steroid from others having the same activity or function". Similarly, the function of generating an immune response or being

"immunostimulatory" does not distinguish any "compound", or oligonucleotide from others having the same activity or function and as such, fails to satisfy the written-description requirement. Applicant has not disclosed any relevant, identifying characteristics, such as structure or other physical and/or chemical properties, sufficient to show possession of the claimed genus. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required. A description of what a material does, rather than what it is, usually does not suffice. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of immunostimulatory oligonucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddles v.Baird*, 30 USPQ2d 1481, 1483. In *Fiddles v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Applicant is reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

13. Claims 26, 28-29, 34, 39-40 and 47-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Schwartz et al [a] (US patent 6,562,798 B1, 6/5/1998).

Schwartz et al [a] teach a method of inducing an immune response and treating cancer in a patient comprising administering an immunostimulatory sequence comprising a central CG sequence, wherein the cytosine is substituted with a modified cytosine or synthetic non-natural nucleosides and wherein the immunostimulatory sequence is conjugated to an antigen or vaccine at the 3' end of the immunostimulatory sequence (see entire document, particularly cols. 3-4, 7, lines 3-6, 9, 10, lines 19-22, 30-33, col. 11, lines 35-49, col. 19, lines 15-21, 35-40, Table 1 and Fig. 1).

Thus, Schwartz et al [a] anticipate the claims.

14. Claims 26, 28-29, 34, 39-40 and 47-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al [b] (WO 99/62923, 12/9/1999, IDS reference filed 2/9/04).

Schwartz et al [b] teach a method of inducing an immune response and treating cancer in a patient comprising administering an immunostimulatory sequence comprising a central CG sequence, wherein the cytosine is substituted with a modified cytosine or synthetic non-natural nucleosides and wherein the immunostimulatory sequence is conjugated to an antigen or vaccine at the 3' end of the immunostimulatory sequence (see entire document, particularly pp. 7-16, 25, 27, Table 1 and Fig. 1).

Thus, Schwartz et al [b] anticipate the claims.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 26, 28-29, 34-35, 39-40 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al [a] (US patent 6,562,798 B1, 6/5/1998) or Schwartz et al [b] (WO 99/62923, 12/9/1999, IDS reference filed 2/9/04) in view of Krieg et al (US Patent 6,207,646 B1, priority at least to 2/7/1995).

Schwartz et al [a] and Schwartz et al [b] have been described supra. Schwartz et al [a] or Schwartz et al [b] do not specifically teach wherein the immunostimulatory

sequence is administered in combination with a chemotherapeutic agent. This deficiency is made up for in the teachings of Krieg et al.

Krieg et al teach a method of treating cancer comprising administering a CpG immunostimulatory oligonucleotide in combination with chemotherapy to increase the responsiveness of the malignant cells and to speed the recovery of the bone marrow through induction of restorative cytokines (see entire document, particularly col. 6, lines 50-58, col. 7, lines 1-5 and col. 33 line 62-67).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method of treating a cancer patient comprising administering an immunostimulatory CpG analog as taught by Schwartz et al [a] or Schwartz et al [b] in combination with a chemotherapeutic agent for therapeutic benefit in cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a method of treating a cancer patient comprising administering an immunostimulatory CpG analog as taught by Schwartz et al [a] or Schwartz et al [b] in combination with a chemotherapeutic agent for therapeutic benefit in cancer patients in view of Krieg et al et al because Schwartz et al [a] or [b] teach a method of treating cancer in a patient comprising administering an immunostimulatory sequence comprising a central CG sequence, wherein the cytosine is substituted with a modified cytosine or synthetic non-natural nucleosides and Krieg et al teach a method of treating cancer comprising administering a CpG immunostimulatory oligonucleotide in combination with chemotherapy to increase the responsiveness of the malignant cells and to speed the recovery of the bone marrow through induction of restorative cytokines. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to combine chemotherapy with an immunostimulatory CpG analog of Schwartz [a] or [b] in order to increase the responsiveness of malignant cells and speed the recovery of the bone marrow through induction of restorative cytokines. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established

scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a method of treating a cancer patient comprising administering an immunostimulatory CpG analog in combination with a chemotherapeutic agent for therapeutic benefit in cancer patients in view of Schwartz et al [a] or Schwartz et al [b] and Krieg et al et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 26, 28-29, 34-35, 39-40 and 47-49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,426,334 in view of Schwartz et al [b] (WO 99/62923, 12/9/1999, IDS

reference filed 2/9/04) and Krieg et al (US Patent 6,207,646 B1, priority at least to 2/7/1995).

Claim 1 of US Patent 6,426,334 is drawn to a method of reducing tumor growth in a mammal having a tumor comprising administering an oligonucleotide having the nucleotide sequence $N_{n1}N_2CpGN_3N_{n4}$, wherein N represents any nucleoside, n1 and n4 each independently represent a number from 0-12 and wherein the cytosine of the CpG dinucleotide has an unmethylated 5-position and wherein at least one N region comprises four contiguous guanosine nucleosides. Claim 1 of US Patent 6,426,334 does not specifically teach wherein the CpG dinucleotide of the immunostimulatory oligonucleotide comprises a modified or non-natural cytosine and a natural or non-natural guanine, and is linked to an antigen or vaccine at the 3'end of the oligonucleotide and wherein the oligonucleotide is administered with a chemotherapeutic agent. These deficiencies are made up for in the teachings of Schwartz et al [b] and Krieg et al.

Schwartz et al [b] have been described supra.

Krieg et al have been described supra.

The claims in the instant application are obvious variants of claim 1 of US Patent 6,426,334 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method of reducing tumor growth in a mammal comprising administering an oligonucleotide having the nucleotide sequence $N_{n1}N_2CpGN_3N_{n4}$ wherein the cytosine is substituted with a modified cytosine or synthetic non-natural nucleoside and the oligonucleotide is linked to an antigen or vaccine at the 3'-end of the oligonucleotide and the oligonucleotide is administered with a chemotherapeutic agent.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a method of reducing tumor growth in a mammal comprising administering an oligonucleotide having the nucleotide sequence $N_{n1}N_2CpGN_3N_{n4}$ wherein the cytosine is substituted with a modified cytosine or synthetic non-natural nucleoside and the oligonucleotide is linked to an antigen or vaccine at the 3'-end of the oligonucleotide and

the oligonucleotide is administered with a chemotherapeutic agent in view of Schwartz et al [b] and Krieg et al because Schwartz et al [b] and Krieg et al teach a method of treating cancer in a patient comprising administering a CpG immunostimulatory sequence, wherein Schwartz [b] teaches the use of modified or non-natural cytosine residues or synthetic non-natural nucleosides and conjugating the immunostimulatory sequence to an antigen or vaccine at the 3'-end of the immunostimulatory sequence and Krieg et al teach combining the immunostimulatory CpG sequence with chemotherapy to increase the responsiveness of the malignant cells and to speed the recovery of the bone marrow through induction of restorative cytokines. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced a method of reducing tumor growth in a mammal comprising administering an oligonucleotide having the nucleotide sequence $N_{n1}N_2CpGN_3N_{n4}$ wherein the cytosine is substituted with a modified cytosine or synthetic non-natural nucleoside and the oligonucleotide is linked to an antigen or vaccine at the 3'-end of the oligonucleotide and the oligonucleotide is administered with a chemotherapeutic agent in view of claim 1 of US Patent 6,426,334 and Schwartz et al [b] and Krieg et al.

Claims 26, 28-29, 34-35, 39-40 and 47-49 are directed to an invention not patentably distinct from claim 1 of commonly assigned US Patent 6,426,334. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned US Patent 6,426,334, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

19. Claims 26 and 34-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 5, 7 and 11-13 of copending Application No. 11/174,002. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of generating an immune response in a vertebrate and treating a vertebrate having cancer comprising administering to the vertebrate animal an immunostimulatory oligonucleotide having the structure 5'-TCTGT**C**GTTCT-X-TCTTG**C**TGTCT-5'; wherein X is a glycerol linker and **C** is 1-(2'-deoxy-β-D-ribofuranosyl)-2-oxo-7-deaza-8-methylpurine and the method further comprises administering a chemotherapeutic agent. Thus, the method of claims 2, 5, 7 and 11-13 of copending Application No. 11/174,002 is a species that reads upon the methods of the present application and hence, are drawn to an invention not patentably distinct from the presently claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 26 and 34-35 are directed to an invention not patentably distinct from claims 2, 5, 7 and 11-13 of commonly assigned copending Application No. 11/174,002. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No. 11/174,002, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can,

under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
Primary Examiner, A.U. 1643